Stroke of Insight

Recognition, Work-Up, and Treatment of Acute Ischemic Stroke

Maksim Kletsel, MD, MS*, Jared Ham, MD

KEYWORDS

• Ischemic stroke • Tenecteplase • Alteplase • Angioedema
• Intracranial hemorrhage • Endovascular therapy

KEY POINTS

- Stroke is the leading neurologic emergency, occurring every 40 seconds, with significant racial disparities in treatment access and outcomes, especially affecting Hispanic and African-American populations.
- Most strokes are ischemic (87%), caused by vascular occlusion due to thrombotic or embolic events, often related to conditions like atherosclerosis, atrial fibrillation, and cardiac sources.
- Quick history-taking (especially last known normal time), physical exam (including cortical signs and NIHSS scoring), and identification of stroke mimics are critical for timely diagnosis and treatment.
- Non-contrast computed tomography is the initial imaging modality, with MRI (diffusion-weighted imaging) providing greater sensitivity for early infarcts. Vessel imaging (computed tomography angiography [CTA]) and perfusion studies help determine eligibility for interventions like thrombectomy.
- Immediate management focuses on maintaining airway, breathing, circulation (ABCs) and blood pressure control. Intravenous (IV) thrombolytics (like alteplase and recently approved tenecteplase) are indicated within specific time windows, with endovascular therapy benefiting patients with large vessel occlusions, even beyond 6 hours in selected cases. Monitoring for complications such as intracranial hemorrhage and thrombolytic-induced angioedema is essential.

INTRODUCTION

In the United States, stroke is the most common neurologic emergency and occurs on average every 40 seconds. It ranks fifth among all causes of death and is a leading cause of long-term disability. The prevalence of stroke is about 3% in the adult population and that is expected to rise by an additional 3.4 million Americans by 2030.[1]

Departments of Emergency Medicine, Neurology, and Rehabilitative Medicine, University of Cincinnati Medical Center, Cincinnati, OH, USA
* Corresponding author. Department of Emergency Medicine, Medical Sciences Building Room 1654, 231 Albert Sabin Way, PO Box 670769, Cincinnati, OH 45267-0769.
E-mail address: kletsemm@ucmail.uc.edu

Emerg Med Clin N Am 44 (2026) 45–69
https://doi.org/10.1016/j.emc.2025.08.004 **emed.theclinics.com**
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Abbreviations	
ACA	anterior cerebral artery
AIS	acute ischemic stroke
AVS	acute vestibular syndrome
BP	blood pressure
CBF	cerebral blood flow
CT	computed tomography
CTP	computed tomography perfusion
DAPT	dual-antiplatelet therapy
DWI	diffusion weighted imaging
ED	emergency department
EVT	endovascular therapy
FLAIR	fluid attenuated inversion recovery
HINTS	Head Impulse, Nystagmus, Test of Skew
ICH	intracranial hemorrhage
IV	intravenous
LKN	last known normal
LVO	large vessel occlusion
MCA	middle cerebral artery
MRP	magnetic resonance perfusion
mRS	modified Rankin score
NIHSS	National Institutes of Health Stroke Scale
r-TPA	recombinant tissue plasminogen activator
s-ICH	symptomatic intracranial hemorrhage
TIA	transient ischemic attack
VAN	vision, aphasia, and neglect

In part due to a rise in the number of stroke centers and utilization of telestroke services, 96% of the US population has access to an emergency department (ED) with stroke capabilities within 1 hour[2] Nonetheless, clear racial disparities exist in stroke care within the United States compared to their White counterparts, Hispanic and African-American patients tend to have lower treatment rates, as well as lower rates of referral to endovascular-capable centers. Additionally, African-American patients are found to have longer ED wait times and time to treatment.[3]

ED visits for stroke are on the rise and the lifetime risk of stroke is only expected to increase with an aging population and accumulation of risk factors.[2,4] It is our duty to be comfortable with the recognition, work-up, and management of a disease process that plagues the communities we serve.

PATHOPHYSIOLOGY

Either through vascular occlusion or bleeding, stroke refers to an interruption in blood flow to brain tissue.[5] While neurons are sensitive to the loss of oxygen and glucose, the initial loss of function is reversible, hence the race to re-establish adequate flow. Unfortunately, if stagnant cerebral blood flow (CBF) persists, this progresses to disruption in membrane function and cell lysis.[6]

Ischemic strokes make up 87% of all strokes.[1] A thrombotic event is the most common underlying mechanism and involves in situ narrowing of the vascular lumen. This is seen with underlying atherosclerosis, as well as arterial dissection, vasculitis, infection, and a hypercoagulable state.[5] In about 20% of cases, the vascular lumen may be obstructed by debris from a more distal source. These emboli may originate in the heart, especially in patients with an underlying cardiac arrhythmia such as atrial fibrillation. Other cardioembolic sources include a mural thrombus, valvular vegetations,

and cardiac tumors.[5] In patients with a cardiac shunt, paradoxic emboli can even arise from the venous system of the pelvis or lower limbs.[7]

Clinical Correlation

A 62 year old female patient presents to the ED with persistent dizziness, as well as associated nausea, since awakening about 1 hour prior. Her vitals are notable for hypertension, but are otherwise unremarkable. Could this be a possible stroke? What specific components of the history and/or physical examination could help you decide?

HISTORY AND PHYSICAL EXAMINATION

History

In a patient with a suspected stroke, the priority is establishing a clear last known normal (LKN) time. Collateral information from bystanders or EMS should corroborate the exact time the patient was last seen symptom-free, rather than the time of symptom onset.[8] Discrepancies in LKN time are common between ED personnel and stroke specialist, which may impact a patient being offered time-sensitive therapies.[9]

Review of a patient's past medical history can screen for pertinent risk factors. More than 90% of stroke risk is attributable to modifiable risk factors.[1] The most important risk factor is hypertension, as well as diabetes, atrial fibrillation, and dyslipidemia. Behavioral risk factors should also be assessed including smoking, alcohol consumption, sedentary lifestyle, and unhealthy diet.[10]

A focused review of the past medical history, recent surgeries, and medications may be used to determine a patient's eligibility for interventions. The remainder of focused history pertaining to the nature of symptoms, coupled with a physical examination, should aim to distinguish a stroke from possible mimics described later.

Examination

On average there is a loss of 1.9 million neurons each minute that a stroke is left untreated.[11] This highlights the importance of a rapid and accurate examination to determine whether a patient's presentation is consistent with a stroke. The presence of cortical signs, especially vision deficits, aphasia, or neglect, can localize an injury to the cerebral cortex. In patients with upper extremity weakness, a *v*ision, *a*phasia, and *n*eglect (VAN) clinical assessment tool was found to be 100% sensitive and highly specific for detecting a large vessel occlusion (LVO).[12] While this screening only takes seconds, it may have implications including prompting timely vessel imaging and contacting a neurointerventionalist.

Presence of lateralizing motor or sensory symptoms is suspicious for a stroke and consideration of neuroanatomy may further assist with localization. A lesion affecting the middle cerebral artery (MCA) may cause contralateral weakness and sensory deficits to the contralateral face and upper extremities, compared to the lower extremities.[5] While the motor weakness may be obvious, more subtle upper extremity weakness may be detected by the presence of a pronator drift.[13] While involvement of the anterior cerebral artery (ACA) may also present with contralateral weakness and sensory findings, these are much more likely to involve the lower extremities. Unlike lesions of the MCA or ACA, lacunar infarcts present with pure motor and/or sensory findings without simultaneous cortical signs.[5]

National Institutes of Health Stroke Scale

The National Institutes of Health Stroke Scale (NIHSS) originated as a research tool and has since become the standard for quantifying stroke severity at the bedside.[14]

The scores range from 0 to 42 and have been validated to correlate with infarct volume and patient outcomes.[14–16] With adequate training, the NIHSS has notable reliability among emergency medicine physicians, neurologists, and nurses.[17,18] To preserve the reproducibility of the scale, it is important to follow the cardinal rules: "score what you see, not what you think," "score the first response, not the best response," and "do not coach."[14]

It is important to know the limitations of the NIHSS, including lower scores for nondominant hemispheric strokes. That is because several testable categories require intact language function.[19] Additionally, the NIHSS is poor at depicting the severity of posterior circulation strokes.[20] Despite accounting for 20% to 25% of ischemic strokes, posterior circulation strokes are frequently misdiagnosed.[21] One reason is that these patients tend to lack the typical hemi-syndromes and cortical symptoms associated with anterior circulation strokes and therefore have lower initial NIHSS scores.[22] Instead, patients with posterior circulation strokes present with vague symptoms including dizziness, headache, and vomiting. In these cases, a physical examination may reveal nystagmus, unsteadiness, ataxia, visual field cut, or dysarthria.[21]

Stroke Mimics

More than 20% of patients who receive intravenous (IV) thrombolytics are ultimately found not to have an ischemic stroke on follow-up imaging.[23] While shorter time to receiving thrombolytics is associated with better outcomes, this needs to be balanced with investing the time to tease out clinical mimics.[24] Seizure, syncope, and functional disorders are most likely to masquerade as a stroke.[25] Patients with stroke mimics tend to be younger and without a history of hypertension, hyperlipidemia, atrial fibrillation, diabetes, or coronary artery disease (**Table 1**).[26]

A thorough examination looking for characteristic clinical signs may be particularly helpful in uncovering certain mimics. Functional neurologic disorder may present with weakness that is mediated by attention, symptom expectation, and patient's beliefs about the illness.[27] When evaluating facial weakness, lip pulling due to ipsilateral contraction of neck muscles is commonly seen in functional disorder. Unlike cortical weakness, functional upper extremity weakness may be detected with downward drift without pronation. Give-away weakness refers to the abrupt loss of tone or strength, such as knee buckling, and suggests likely underlying functional weakness. Additional tests can highlight the discrepancy between voluntary and involuntary movements common to functional disorder. For instance, Hoover's sign (placing a hand under the heel of the patient's seemingly weak leg while they attempt to lift the opposite leg against resistance) detects unattended hip extension in the reportedly weak leg when the contralateral hip is actively flexed.[28]

Careful assessment of an acute facial palsy can distinguish a peripheral etiology, such as Bell's palsy, from a stroke. The muscles of the upper and lower face receive motor innervation from the facial nerve. Patients with a peripheral nerve palsy will commonly present with a facial droop, as well as inability to close their eyes and effacement of forehead wrinkles. Meanwhile, if the facial paralysis spares the forehead, a stroke should be suspected. This is because an ischemic insult is likely to only disrupt one of motor cortices that supply the dual innervation of the upper facial muscles.[29]

Stroke Chameleons

When considering medical malpractice cases relating to acute stroke in the ED, the most common allegations involve misdiagnosis and failure to appropriately treat.[30] Atypical or subtle symptoms are especially likely to be disregarded as a possible

Table 1
Common "S" stroke mimics and their distinguishing features from a stroke[25,91–94]

Stroke Mimics	Comments	Distinguishing Features from a Stroke
Seizure	Most common stroke mimic (~20%).	• Transient focal negative symptoms may follow a seizure and mimic a stroke ○ Commonly have a past history of epilepsy ○ May present with motor symptoms (Todd's paralysis) ○ May also have additional focal symptoms (sensory disturbances, gaze palsy, aphasia, etc.) ○ These symptoms are typically transient and last a few minutes • Occasionally a seizure can occur at the time of stroke onset ○ Occurs in up to 6.2% of ischemic strokes ○ Establish if negative symptoms occurred prior to the seizure
Syncope	Stroke is rarely the cause of a syncopal event. Notable exceptions include subclavian steal syndrome and Wallenberg syndrome.	• Consider a stroke when significant neurologic symptoms occur before the episode or persist during the recovery period
Sepsis/Infection	Infection may lead to encephalopathy and may present as weakness, coma, and speech changes. Recrudescence of prior stroke-related deficits can also occur in the setting of metabolic, infectious, and toxic dysfunction. Recall that sepsis can also lead to a hypercoagulable state and increase risk of a true ischemic stroke.	• When due to infection, these symptoms are typically gradual in onset ○ Less likely to be abrupt onset with focal deficits ○ Look for an infectious process such as fever and tachycardia
Sugar Levels	Both hypo- and hyperglycemia may lead to neurologic symptoms and even focal deficits. Blood glucose level should be considered in patients with a neurologic complaint	• Neuroglycopenic episodes commonly present with confusion with associated autonomic symptoms ○ Diaphoresis and tachycardia are typically first to occur ○ Hemiparesis can occur when glucose levels are severely low (usually <30 mg/dL)

(*continued on next page*)

Table 1
(continued)

Stroke Mimics	Comments	Distinguishing Features from a Stroke
Severe Headaches/ Migraines	Migraines with aura account for 20%–30% of headaches and commonly present with visual symptoms, as well as possible sensory or other central nervous system (CNS) symptoms. Basilar migraines may present with visual disturbances, ataxia, and dysarthria often mimicking a posterior circulation stroke. Hemiplegic migraines are especially rare, but present with unilateral motor weakness that may last for hours to days.	• Consider migraine as underlying etiology in patients with a prior personal/family history of migraines/headaches ○ Also have typical classic migraine symptoms • Aura symptoms typical start prior to the headache and most commonly involve visual symptoms ○ Gradual in onset over several minutes ○ May extend into the headache phase and even last after the headache resolves
Space-Occupying Lesion	This includes CNS tumors, metastases, and abscesses. Neurologic symptoms may occur due to compressive effects of tumor on vascular bed, as well as underlying hemorrhage and/or tumor embolus.	• Neurologic findings are typically gradual in onset over 24–48 h

From[25,91–94]

stroke in a rushed ED encounter. Unfortunately, failure to diagnose these "stroke chameleons" may lead to delayed treatment and worse patient outcomes.[31]

One of the most common missed stroke presentations involves those with altered mental status.[32] Bilateral thalamic and brainstem strokes are known to cause reduced degree of consciousness.[33] Additionally, strokes involving the non-dominant hemisphere may cause inattentiveness, lack of emotion/empathy, inability to understand non-verbal communication, and lack of prosody of speech. Specifically, insult to the non-dominant temporoparietal region may lead to loss of spatial orientation and inability to recognize faces, objects, and places.[34] These symptoms can erroneously be attributed to metabolic disturbances, infection, hypertensive encephalopathy, or even psychiatric disease.[35]

Dizziness accounts for 4% of all ED chief complaints and while most causes are benign, it is the most common symptom in patients with a posterior circulation stroke.[21,36] When encountering a patient with dizziness, a structured approach is helpful to delineate a subtle stroke chameleon from more benign causes (**Table 2**).

Patients with acute vestibular syndrome (AVS) present with continuous symptoms that are even present at rest. In those patients, a 3 part Head Impulse, Nystagmus, Test of Skew (HINTS) examination performed by trained clinicians has a high sensitivity for stroke and may outperform an early MRI.[37] Recent GRACE-3 guidelines support the use of a HINTS examination, coupled with testing for unilateral hearing loss, in patients with AVS and nystagmus. For those patients with continuous symptoms without nystagmus, gait unsteadiness can help distinguish a stroke from peripheral causes. These patients should all be screened for the "deadly D's" associated with

Table 2
Features, causes, and proposed work-up of 3 distinct clinical syndromes involving patients with symptoms of dizziness and/or vertigo[21,36]

Clinical Syndrome	Presentation	Common Benign Causes	Key Dangerous Causes	Recommended Work-up

Acute Vestibular Syndrome (AVS)	• May start with trigger
	  ○ Symptomatic even at rest
	• Acute onset and continuous symptoms
	  ○ Lasting >24 h
	• Associated with nausea, vomiting, postural instability, nystagmus
		Labyrinthitis, vestibular neuritis	Posterior circulation stroke/ TIA	• Use HINTS testing
				  ○ Test of hearing can be added (HINTS plus)
				• Next best available test is MRI-DWI

Spontaneous Episode Vestibular Syndrome (SEVS)	• No clear trigger
	  ○ Asymptomatic at rest
	• Transient episodes
	  ○ Lasting minutes to hours
	• Associated with nausea, vomiting, postural instability, nystagmus
		Vestibular migraine, Meniere disease	Posterior circulation TIA	• History can usually tease out a TIA from a more benign cause

Triggered Episode Vestibular Syndrome (TEVS)	• Have a clear positional trigger
	  ○ Such as head movement or standing
	  ○ Asymptomatic at rest
	• Brief transient episodes
	  ○ Lasting seconds to minutes
	• Associated with nausea, vomiting, postural instability
		Benign paroxysmal positional vertigo (BPPV), orthostatic hypotension	Central paroxysmal positional vertigo (CPPV) from structural central lesions	• Consider a Dix-Hallpike test for BPPV
				• If concern for central cause consider an MRI-DWI

From Pelletier J, Koyfman A, Long B. Pearls for the emergency clinician: Posterior circulation stroke. J Emerg Med. 2023;65(5):e414–e426. https://doi.org/10.1016/j.jemermed.2023.07.007; Edlow JA, Carpenter C, Akhter M, et al. Guidelines for reasonable and appropriate care in the emergency department 3 (GRACE-3): Acute dizziness and vertigo in the emergency department. Acad Emerg Med 2023;30(5):442–86. https://doi.org/10.1111/acem.14728.

a stroke, including diplopia, dysarthria, dysphagia, dysphonia, dysmetria, and dysesthesia. In cases where central cause is suspected or HINTS examination is equivocal, MRI/MRA should be pursued due to the poor sensitivity of computed tomography (CT)/CTA for posterior circulation strokes.[36]

Patients in whom stroke was missed tend to have fewer risk factors including younger age, lower use of lipid-lowering medications, and lower blood pressure (BP) on admission. Furthermore, these patients tend to less frequently present with eye deviation, paresis, or sensory deficits.[38] This highlights how overreliance on cardiovascular risk profile and presence of lateralizing symptoms may lead to missed stroke. Instead, clinicians should stay vigilant when faced with atypical symptoms with a low threshold to initiate a broad work-up and obtain expert consultation.

Clinical correlation

Our patient awoke with symptoms and has an unclear time of symptom onset, yet presence of continuous symptoms and findings from a HINTS examination are concerning for a possible stroke. What are your priorities at this time? Which laboratory tests and imaging modalities are you ordering?

WORK-UP OF SUSPECTED STROKE

Priorities in the Emergency Department

When a patient presents with a possible acute stroke, the initiation of imaging needs to be performed as soon as possible and ideally within 20 minutes of arrival to the ED. A blood glucose level should be emergently obtained as a level less than 50 mg/dL is a contraindication to IV thrombolytics. Other laboratory tests should include a complete blood count, serum electrolytes, plus renal function and coagulation tests (prothrombin time [PT], international normalized ratio [INR], activated partial thromboplastin time [aPTT]). Remainder of testing may be tailored to the patient, such as an assay to detect anticoagulant effects, toxicologic screen, and/or pregnancy testing. Due to association between stroke and cardiac anomalies, baseline cardiac markers and electrocardiogram should be performed in all patients with suspicion of stroke.[39]

Imaging Modalities

Non-contrast computed tomography

A non-contrast enhanced CT scan of the brain is the first-line imaging modality ordered for most patients presenting to the ED with a possible stroke. It is primarily used to detect the presence of an intracranial hemorrhage (ICH), which is a contraindication to thrombolytic therapy, as well as the presence of tumors and intracranial abscesses that may mimic stroke symptoms.[5] It can also help identify early ischemic changes that may be seen in AIS using the Alberta Stroke Program Early Computed Tomography Score. This score ranges from 0 to 10 and points are deducted when there is a loss of gray–white matter distinction detected on CT pertaining to particular regions of the MCA territory.[40] A lower score indicates presence of more intraparenchymal hypoattenuation and concern for early potential development of irreversible injury.[41]

Diffusion-weighted MRI

While CT is readily available, diffusion-weighted MRI is more sensitive at detecting an acute infarct and is especially useful in patients who have unclear LKN.[42] Diffusion-weighted imaging (DWI) detects the movement of water protons, which quickly becomes restricted in ischemic brain tissue.[43] Meanwhile, vasogenic edema appears more gradually and is detected several hours after stroke onset on fluid attenuated

inversion recovery (FLAIR) imaging.[44] A DWI–FLAIR mismatch can identify hyperacute strokes within 3 and 4.5 hours of onset.[45] As discussed later, this is especially useful to assess for thrombolytic candidacy in patients whose LKN is unclear (Fig. 1).

Computed tomography or MR angiography

Vessel imaging is useful in identifying an occlusion and/or stenosis within the vasculature of the head or neck, which may explain the patient's symptoms. This is typically performed in conjunction with a non-contrast enhanced CT to assess eligibility for endovascular therapy (EVT). If not obtained simultaneously, obtaining angiography should never delay administration of IV thrombolytics in patients who would otherwise qualify.[5]

Perfusion imaging

Perfusion imaging involves either computed tomography perfusion (CTP) or magnetic resonance perfusion (MRP) imaging modalities to distinguish an infarcted core versus the surrounding penumbra. While MRI detects restriction of water movement in infarcted tissue, CTP identifies reduced CBF less than 30% to detect an ischemic core. To localize tissue at risk, both CTP and MRP use various perfusion parameters to detect a perfusion deficit compared to normal brain tissue. The mismatch between the core and perfusion deficit volume is a surrogate for the amount of salvageable brain tissue.[46] While perfusion imaging is not performed routinely on all patients with a stroke, it is useful for determining eligibility for thrombectomy in patients with LVO presenting 6 to 24 hours from LKN (Fig. 2).

MANAGEMENT OF ISCHEMIC STROKE

General Management

Airway, breathing, circulation

As with any critically ill patient, the primary focus of managing acute ischemic stroke (AIS) should always be on assessing and maintaining the patient's airway, breathing, and circulation. Patients with an AIS may require intubation due to a myriad of reasons, including reduced level of alertness, bulbar dysfunction, need to facilitate imaging/

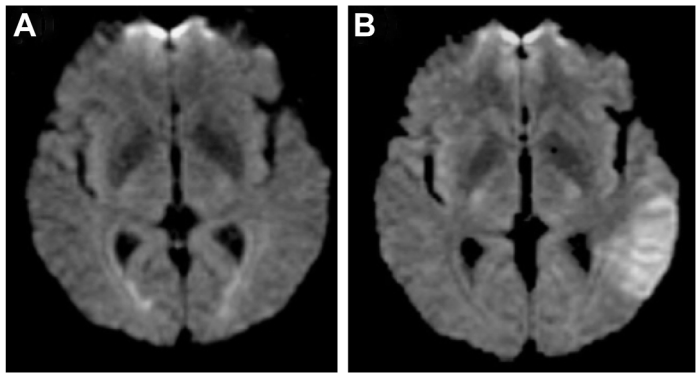

Fig. 1. DWI–FLAIR mismatch may be used to detect hyperacute ischemic strokes in patients with unclear last known well. (*A*) No FLAIR signal detected. (*B*) Hyperintense lesion seen on diffusion-weighted imaging in the left temporal lobe consistent with a hyperacute infarct due to lack of corresponding signal on FLAIR. (*From* Warach S. Use of diffusion and perfusion magnetic resonance imaging as a tool in acute stroke clinical trials. Curr Control Trials Cardiovasc Med. 2001;2(1):38–44. https://doi.org/10.1186/cvm-2-1-038.)[95]

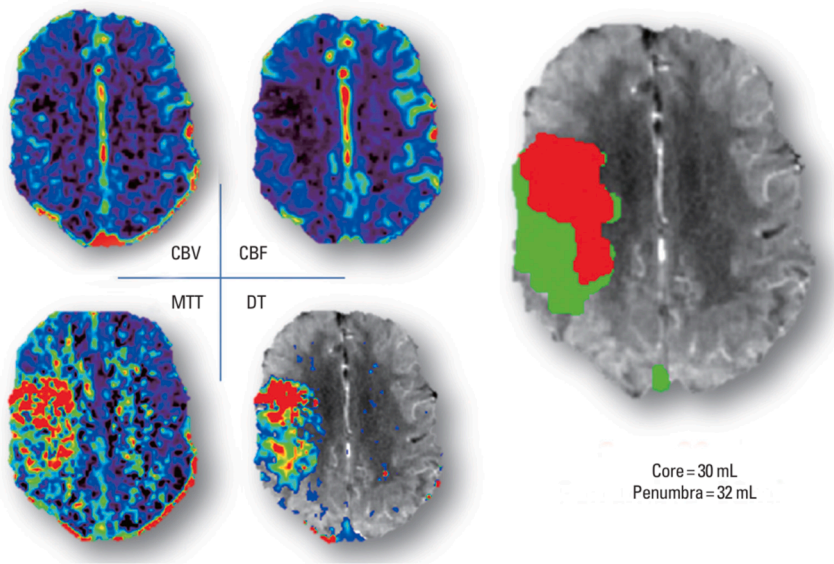

Fig. 2. CT perfusion imaging measures perfusion parameters including cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and delay time (DT) to distinguish normal tissue, from infarcted tissue (*red*), and at-risk penumbra (*green*). (*From* Lin L, Bivard A, Parsons MW. Perfusion patterns of ischemic stroke on computed tomography perfusion. J Stroke. 2013;15(3):164–173. https://doi.org/10.5853/jos.2013.15.3.164.)[96]

transport, and/or anticipated clinical course. When intubating a patient with a suspected brain ischemia, it is critical to avoid hypotension and compromising the much-needed blood flow to the ischemic penumbra. A mean arterial pressure (MAP) greater than 80 mm Hg should be maintained throughout the pre-intubation and post-intubation period. This may require IV fluids and/or vasoactive medications to achieve. Furthermore, induction agents such as etomidate or ketamine should especially be considered due to their favorable hemodynamic profiles[47]

Supplemental oxygen is only recommended to maintain SpO2 >94%.[5] This is because hypoxia is a known culprit of secondary brain injury, but excess hyperoxia can actually worsen reperfusion injury. Clinicians should be judicious about use of supplemental oxygen to stroke patients and diligent about adjustments to ventilator settings. Additionally, carbon dioxide is known to hinder CBF via vasoconstriction. Efforts should be made to maintain eucapnia as well, with a target P_{CO_2} of 30 to 40 mm Hg.[47]

Blood pressure

While hypotension may threaten the vulnerable penumbra, pre-treatment and post-treatment hypertension has been associated with increased risk of ICH in those receiving thrombolytics.[48,49] Current AHA/ASA guidelines recommend maintaining a BP less than 185/110 mm Hg in patients with AIS who are eligible for IV thrombolysis and/or thrombectomy (**Table 3**).[39]

Hypertension is common in AIS and occurs for multiple reasons including dynamic changes to ensure cerebral perfusion in LVOs. This is the basis for allowing "permissive hypertension" in patients who are ineligible for reperfusion therapy.[50] Nonetheless, stroke patients may have impaired ability to maintain constant CBF over a

Table 3
Treatment options to meet blood pressure goals of less than 185/110 mm Hg in stroke patients eligible for reperfusion therapy[5,39]

Treatment Options to Lower Blood Pressure Prior to Reperfusion Therapy	
Labetalol	• 10–20 mg IV over 1–2 min • May repeat one time
Nicardipine	• 5 mg/h IV • Titrate up by 2.5 mg/h ever 5–15 min • Max dose 15 mg/h
Clevidipine	• 1–2 mg/h IV • Titrate by doubling dose every 2–5 min • Max dose 21 mg/h
Other Agents to Consider	• Hydralazine • Enalaprilat • IV Sodium Nitroprusside

From Go S, Kornegay J. Stroke syndromes. In: Tintinalli JE, Ma OJ, Yealy DM, et al, eds. Tintinalli's emergency medicine: A comprehensive study guide, 9e. New York, NY: McGraw-Hill Education; 2020. https://accessmedicine.mhmedical.com/content.aspx?aid=1209938893. Accessed 2025/02/28; Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the american heart association/ american stroke association. Stroke 2019;50(12):e344–e418. https://doi.org/10.1161/STR.0000000000000211.

range of cerebral perfusion pressure. This altered cerebral autoregulation mechanism limits the degree that arterioles can contract in response to higher pressures until giving way to passive vasodilation, leading to increased CBF and disruption of the blood brain barrier.[51] For patients ineligible for reperfusion therapy, current guidelines suggest early treatment of hypertension only for BP $\geq$220/120 mm Hg or those with comorbidities warranting lower BP targets.[39]

Clinical correlation. Though our patient has an unclear LKN, an MRI of the brain does reveal a lesion on DWI, without a correlating FLAIR signal, in the posterior circulation. Vessel imaging does not reveal an LVO. Her blood glucose level is 67 mg/dL and INR is noted to be 1.5. Does she qualify to receive IV thrombolytic therapy? How would you counsel her about potentially receiving systemic thrombolytics?

IntravenousThrombolytics

Alteplase

The basis of IV thrombolytic therapy in the management of AIS is that arterial thrombi are composed of aggregated platelets and fibrin.[52] In the setting of cerebral ischemia, there is an endogenous release of plasminogen activators in an attempt to maintain vascular patency.[53] These enzymes facilitate the formation of plasmin, from its inactive plasminogen form, which promotes local fibrinolysis by solubilizing fibrin within a clot.[52]

Alteplase was the first recombinant tissue plasminogen activator (r-tPA) to receive FDA-approval for management of AIS.[5] This was based on the landmark NINDS trial which found that patients with an AIS who received r-tPA within 3 hours of symptom recognition had improvement in clinical outcome compared to placebo. More specifically, the study concluded that patients receiving r-tPA were at least 30% more likely to have minimal or no deficits at 90 days.[54]

Tenecteplase

Tenecteplase (TNK) facilitates fibrinolysis similar to alteplase. However, TNK is more fibrin specific and more resistant to plasminogen activator inhibitor-1. This leads to a longer half-life compared to r-tPA (20–24 mins vs 3–5 mins), allowing the benefit of TNK to be administered as a single bolus rather than a prolonged infusion.[55]

Several trials have demonstrated that TNK is noninferior compared to r-tPA in patients with AIS presenting within 4.5 hours of symptom recognition. When TNK was dosed at 0.25 mg/mg, these studies demonstrated that it had a similar safety profile compared to r-tPA, including similar rates of symptomatic intracranial hemorrhage (sICH) and all-cause mortality.[56,57] When coupled with mechanical thrombectomy, TNK may even be superior at successful vessel recanalization.[58] Current AHA/ASA guidelines suggest that TNK may be utilized as an alternative to r-tPA as a bridging therapy prior to thrombectomy.[39] European societal organizations have also endorsed the use of TNK as an alternative to r-tPA in treatment in AIS even in patients not receiving mechanical thrombectomy.[59,60]

TNK was granted FDA approval in early 2025 for use in AIS, making it the first new medication approved for AIS in nearly 3 decades. Hospitals will likely transition to this agent given its ease of use, cost of effectiveness, and noninferiority to alteplase (Table 4).

Indications

It is estimated that approximately 6% to 8% of all strokes are eligible for IV thrombolytic therapy, and delay to medical presentation is the most common reason for exclusion.[61] When evaluating these patients in the ED, establishing a reliable LKN time is critical to determining eligibility. If a clear timeframe cannot be established, the patient may not be eligible for IV thrombolysis.[39]

Less than 3 hours from last known normal

When presenting within 3 hours from LKN, IV thrombolysis is recommended regardless of NIHSS score if the stroke symptoms are deemed to be disabling. Even if symptoms are gradually improving but are still disabling, IV thrombolysis is still recommended (Table 5).

Table 4
Comparison of alteplase and tenecteplase for treatment of acute ischemic stroke[97]

	Alteplase (r-tPA)	Tenecteplase (TNK)
Fibrin Specificity	Less specific	14–15x more specific to fibrin
Degradation	Less resistant	More resistant to plasminogen tissue inhibitor-1
Half-life Elimination	5 min	20–24 min
FDA-Approved Indications	Acute Ischemic Stroke Acute Myocardial Infarction Pulmonary Embolism	Acute Ischemic Stroke Acute Myocardial Infarction
Acute Ischemic Stroke Dose	0.1 mg/kg bolus, then 0.8 mg/kg infusion over 60m (max dose of 90 mg)	0.25 mg/kg bolus (max dose of 25 mg)

Rodriguez M, Sidebottom C, Wells DA, et al. A systematic review of the efficacy and safety of tenecteplase versus alteplase in acute ischemic stroke: A time to pass the torch. Stroke: Vascular and Interventional Neurology 2024;4(4):e001110.

Table 5
Inclusion criteria for IV thrombolytic administration for less than 3 h from symptom onset[39]

Symptom Onset <3 h	Eligibility for IV Thrombolytics: • Age ≥18 y • No NIHSS Score Cut-off if Symptoms are disabling • Even if Symptoms are improving, Still eligible if Symptoms are disabling

From Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the american heart association/ american stroke association. Stroke 2019;50(12):e344–e418. https://doi.org/10.1161/STR.0000000000000211.

When counseling patients on administration of IV thrombolytics, it is important to consider the benefits as well as the potential risks. Based on the NINDS data, patients who received r-tPA within 3 hours of LKN time had a 13% absolute benefit based on improvement in stroke scale at 3 months. It is also important to consider that patients receiving r-tPA were also more prone to asymptomatic ICH (4.4% vs 2.9% with placebo) and symptomatic ICH (6.4% vs 0.64% with placebo).[54] To help patients and their families better conceptualize and make informed decisions, these data can be further extrapolated to a treatment group consisting of 100 people. Of 100 patients who received r-tPA for AIS within 3 hours of symptom recognition, about 32 patients benefited in an important manner. Meanwhile, approximately 3 out of those 100 people had a worse outcome because of the treatment.[62]

Three to 4.5 hours from last known normal

In 2008, the ECASS III trial sought to establish the safety and efficacy of systemic thrombolytics when the administration time was extended beyond the typical 3 hours and up to 4.5 hours from LKN. When evaluating disability at 90 days, those patients who received r-tPA had a more favorable outcome compared to placebo. Furthermore, despite a higher incidence of ICH, including sICH, the incidence of mortality did not differ significantly between the two groups.[63]

It is important to be familiar with the inclusion criteria of this trial, including age 80 years or less, NIHSS 25 or less, no history of diabetes or prior stroke, not taking an oral anticoagulant, and ischemic injury not involving more than a third of the MCA territory.[63] The most recent AHA/ASA stroke guidelines support the use of IV thrombolytics in the extended 3 to 4.5 hour time window for select patients who meet the criteria above.[39] When evaluating a patient with a disabling ischemic stroke and symptom onset time between 3 and 4.5 hours, who do not necessarily meet the inclusion criteria, it is recommended to discuss the utility of IV thrombolytics with a stroke specialist (**Table 6**).

Greater than 4.5 hours from last known normal

At this time, the utility of IV thrombolytic administration for AIS beyond the 4.5 hour window has not been well established. The TIMELESS trial involved 458 patients who received TNK or placebo between 4.5 and 24 hours after symptom recognition. Despite similar rates of sICH between the two groups, the study did not find any benefit in functional outcomes in those who received IV thrombolysis.[64] Meanwhile, another trial actually did find lower modified Rankin scores (mRS) at 90 days, with higher rates of sICH, in patients who received TNK beyond 4.5 hours of symptom recognition compared to placebo.[65] Due to mixed available data, current guidelines

Table 6
Inclusion criteria for IV thrombolytic administration for acute ischemic stroke up to 4.5 h from symptom onset[39]

Symptom Onset Within 3–4.5 h	Eligibility for IV Thrombolytics: • Age ≤80 year[a] • No history of diabetes or prior stroke[a] • NIHSS Score ≤25[b] • Not taking an anticoagulant • Without imaging evidence of ischemic injury involving >1/3 of the MCA territory

[a] May be beneficial for older patients and those with a history of diabetes or prior stroke.
[b] Uncertain benefit if administered for more severe strokes (NIHSS score>25).
From Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2019;50(12):e344–e418. https://doi.org/10.1161/STR.0000000000000211.

do not recommend administration of IV thrombolytics if LKN time extends beyond 4.5 hours.[39]

Awakening with symptoms

When a patient awakens with concerning symptoms, it is often difficult to elucidate the exact time of onset. In such cases, an MRI may be used to evaluate for the presence of an acute ischemic infarct and determine eligibility for treatment in patients who would otherwise be ineligible.

In the WAKE-UP trial, patients with stroke symptoms of unknown onset time and a DWI–FLAIR mismatch on MRI were randomly assigned to receive either r-tPA or placebo. Those assigned to receive the thrombolytic had a better functional outcome as noted by a lower median mRS at 90 days. There were also no statistically significant differences in rate of sICH or mortality between the two groups.[66] A meta-analysis of 4 similar trials, including the WAKE-UP trial, also found significantly better functional outcomes for patients with unclear LKN and DWI-FLAIR mismatch who received r-tPA. While patients who received r-tPA had higher rates of sICH, they were less likely to suffer severe disability or death compared to placebo (**Table 7**).[67]

Contraindications

Once a patient is determined to be eligible to receive IV thrombolytics there are certain contraindications that need to be carefully considered. These can be broadly grouped

Table 7
Inclusion criteria for administration of IV thrombolytics for patients who awaken with stroke symptoms and have an unclear last known well[39]

Awakening with stroke symptoms	Eligibility for IV Thrombolytics: • Within 4.5 h of Symptom recognition • Mismatch between MR DWI and FLAIR • MR DWI lesion is less than one-thirdof MCA territory

From Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2019;50(12):e344–e418. https://doi.org/10.1161/STR.0000000000000211.

into 3 categories to make them easier to recall and highlight the reasoning behind the exclusion criteria. One of the most common clinical conundrums is the eligibility for patients taking anticoagulation to receive IV thrombolytics. As noted later, patients who are prescribed various forms of anticoagulation may still be eligible based on the timing of their last dose of medication and results of coagulopathy studies.[39]

Complications

Post-thrombolytic intracranial hemorrhage

Hemorrhage is a feared complication of administration of IV thrombolytics and is associated with poor and fatal outcomes.[68] The incidence of sICH in stroke patients receiving IV thrombolytic therapy is reported to be between 2% and 7%.[69] Stroke severity, as determined by NIHSS score, is one particular risk factor that is robustly associated with an increase in sICH risk. Other risk factors include older age, higher baseline glucose, hypertension, congestive heart disease, renal failure, ischemic heart disease, atrial fibrillation, baseline antiplatelet use, and visible acute infarct on imaging.[69]

The underlying pathophysiology of post-thrombolytic ICH is multifactorial. Thrombolytics function to restore intracranial blood flow through the degradation of fibrin within a clot. This leads to consumptive coagulopathy through the depletion of fibrinogen. Patients with stroke receiving thrombolytics are often found to have low serum fibrinogen levels, which correlates to an increased risk of sICH.[70] In addition to thrombolytic-associated coagulopathy, thrombolytics also increase the risk of sICH by likely playing a role in disruption of the blood brain barrier and inducing reperfusion injury to injured brain tissue.[71]

In the original landmark NINDS trial, all fatal sICH occurred in the first 24 hours after receiving thrombolytics. Even more pertinent to emergency medicine clinicians, 80% of these fatal sICH occurred in the first 12 hours.[54] As a result, it is important to be familiar with post-thrombolytic monitoring as these patients commonly reside in the ED pending availability of a stroke bed. Current AHA/ASA guidelines recommend for BP to be monitored every 15 minutes for the first 2 hours and a target of less than 180/105 mm Hg for the initial 24 hours.[39] This is because post-thrombolysis elevation of BP is associated with development of sICH.[68] Guidelines also suggest for neurologic assessments to be performed at the same frequency. Any worsening in neurologic examination, as well as severe headache, acute hypertension, nausea, or vomiting, should raise suspicion for a post-thrombolytic hemorrhage.[39]

If a post-thrombolytic hemorrhage is suspected, further drug administration should be halted, and initial management should focus on the patient's airway, breathing, and circulation. Laboratory studies should be ordered, including a CBC, coagulation studies, fibrinogen level, and type & screen. As soon as clinically able, an emergent non-contrast enhanced CT scan of the head needs to be obtained.[5]

If an ICH is confirmed, a neurosurgery consult is appropriate to determine if the patient is a candidate for a surgical clot evacuation and/or decompressive craniectomy. Medical management should focus on preventing further hematoma expansion as this is a major predictor of death and disability.[69] While BP control is one fundamental pillar of prevention of hematoma expansion, exact treatment targets remain elusive. An RCT involving patients with ICH compared intensive treatment (systolic BP goal <140 mm Hg) to a control group (target systolic BP goal <180 mm Hg) and found that patients in the intensive treatment group had improved functional outcomes as well as better physical and psychological well-being. Nonetheless, there was no difference in mortality or nonfatal serious adverse events between the two groups.[72] Meanwhile, a more

recent RCT found no difference in mRS or rate of death/disability in ICH patients in the intervention group (SBP 110–139 mm Hg) compared to control group (140–179 mm Hg). That study also found a higher rate of renal-related adverse events at 7-days in the intervention group.[73] AHA/ASA guidelines for ICH support targeting a systolic BP goal of 140 mm Hg and maintaining systolic BP between 130 to 150 mm Hg within 1 hour of treatment initiation. Lowering the SBP less than 130 mm Hg is not recommended, and wide fluctuation in BP should be avoided.[74]

Additional treatment options to prevent hematoma expansion include cryoprecipitate, which is derived from fresh-frozen plasma and contains fibrinogen to correct the presumed hypofibrinogenemia that may be caused by IV thrombolytics.[69] Unfortunately, cryoprecipitate requires thawing and may not be as readily available. Other therapies may include antifibrinolytics such as tranexamic acid and ε-aminocaproic acid. These agents are more easily available, have a rapid onset, and directly oppose the activity of thrombolytics through inhibition of plasmin.[69] Current guidelines support the use of either of these agents in the setting of thrombolytic-induced sICH, especially if obtaining cryoprecipitate is delayed or treatment with blood products is not an option.[39]

Historically, platelet transfusions have been recommended for post-thrombolytic hemorrhage, due to suspicion that these agents contribute to platelet inhibition.[69,75] Recent studies have demonstrated that platelet transfusions may actually increase hematoma size and current guidelines suggest that platelet transfusions be reserved for patients with thrombocytopenia or those having surgery.[69,74] Other treatment options include prothrombin complex concentrates, fresh-frozen plasma, and vitamin K. In general, the use of these adjuncts in sICH is controversial and typically only considered for patients already on anticoagulation therapy prior to receiving thrombolytics (**Fig. 3**).[69]

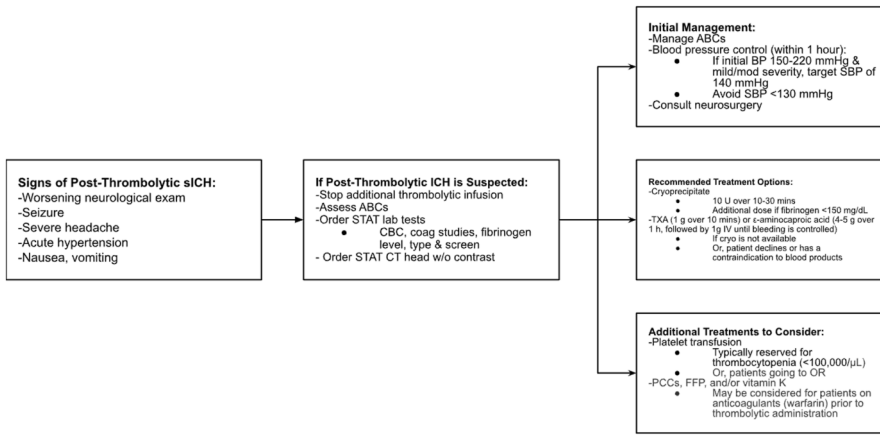
Signs of Post-Thrombolytic sICH:
-Worsening neurological exam
-Seizure
-Severe headache
-Acute hypertension
-Nausea, vomiting
If Post-Thrombolytic ICH is Suspected:
-Stop additional thrombolytic infusion
-Assess ABCs
-Order STAT lab tests
• CBC, coag studies, fibrinogen level, type & screen
- Order STAT CT head w/o contrast
Initial Management:
-Manage ABCs
-Blood pressure control (within 1 hour):
• If initial BP 150-220 mmHg & mild/mod severity, target SBP of 140 mmHg
• Avoid SBP <130 mmHg
-Consult neurosurgery
Recommended Treatment Options:
-Cryoprecipitate
• 10 U over 10-30 mins
• Additional dose if fibrinogen <150 mg/dL
-TXA (1 g over 10 mins) or ε-aminocaproic acid (4-5 g over 1 h, followed by 1g IV until bleeding is controlled)
• If cryo is not available
• Or, patient declines or has a contraindication to blood products
Additional Treatments to Consider:
-Platelet transfusion
• Typically reserved for thrombocytopenia (<100,000/μL)
• Or, patients going to OR
-PCCs, FFP, and/or vitamin K
• May be considered for patients on anticoagulants (warfarin) prior to thrombolytic administration

Fig. 3. Assessment and management of post-thrombolytic intracranial hemorrhage.[69,74] (*From* Yaghi S, Willey JZ, Cucchiara B, et al. Treatment and outcome of hemorrhagic transformation after intravenous alteplase in acute ischemic stroke: A scientific statement for healthcare professionals from the american heart association/american stroke association. Stroke 2017;48(12):e343–e361. https://doi.org/10.1161/STR.0000000000000152; Greenberg SM, Ziai WC, Cordonnier C, et al. 2022 guideline for the management of patients with spontaneous intracerebral hemorrhage: A guideline from the american heart association/american stroke association. Stroke 2022;53(7):e282–e361. https://doi.org/10.1161/STR.0000000000000407.)

Clinical correlation. Our patient opts to receive IV thrombolysis. Unfortunately, while awaiting a bed in the neuroscience intensive care unit, she develops a profound change to her speech. Prior to ordering an STAT CT scan you examine the patient and find unilateral swelling of the tongue and both lips. What is likely causing this patient's symptoms? How do you determine whether this patient needs intubation? What are some other treatment options you might consider?

Thrombolytic-Induced Angioedema

Angioedema is characterized by formation of non-pitting edema in the subcutaneous or submucosal tissues, frequently involving the face, neck, gastrointestinal tract, or distal extremities.[76] IV thrombolytics are known culprits of medication-induced angioedema. The incidence may be as high as 5.1% and there is a 6 times higher risk in those concomitantly taking an ACE-inhibitor.[5,77–79]

The pathophysiology appears to center around formation of plasmin by thrombolytics which leads to the downstream formation of a potent vasodilator known as bradykinin. The complement system is also activated by plasmin and functions to degranulate mast.[80] These pathways lead to increased vascular permeability, vasodilation, and accumulation of interstitial fluid that yields to the characteristic swelling.[81]

Patients typically develop unilateral swelling that is often isolated to the anterior oropharynx, lips, and tongue.[77] While most cases are mild and resolve spontaneously within 24 hours, clinicians need to be especially vigilant about monitoring the patient's airway. Rapid progression of swelling within 30 minutes, as well as involvement of the larynx, palate, floor of mouth, or oropharynx, increase the likelihood of need for intubation. Current guidelines do support the use of antihistamines, IV steroids, and intramuscular epinephrine for worsening symptoms.[39] However, it is important to be aware that these therapies may not be effective as they fail to address the predominant bradykinin pathway.[81] More specific therapies may include fresh frozen plasma, as it contains enzymes that can degrade bradykinin, as well as a direct bradykinin receptor antagonist (icatibant), and C1 esterase inhibitor that prevents addition bradykinin formation from kallikrein.[77,81]

Endovascular Therapy

Less than 6 hours from last known normal

Following IV thrombolytics, EVT involving mechanical clot and/or direct intra-arterial thrombolysis was the next revolution in AIS management. The MR CLEAN trial demonstrated that in patients with a proximal LVO of the anterior circulation, EVT performed within 6 hours of LKN improved functional recovery compared to standard care alone. About 90% of the patients who underwent EVT also received IV thrombolysis and there were no differences in adverse events between the two groups.[82] Current guidelines recommend EVT for proximal anterior circulation occlusions in patients presenting within 6 hours of LKN. EVT may even be considered for patients with more distal occlusions, including M2/M3 and the posterior circulation (**Fig. 4**).[39]

SixTo 24 hours from last known normal

The boundaries were further pushed in the DAWN trial where EVT was offered to patients with an LVO who presented beyond 6 hours from LKN. This study utilized diffusion-weighted MRI or perfusion CT to determine a favorable mismatch between at-risk penumbra and infarcted core. It found that in those with symptom onset of 6 to 24 hours and a favorable mismatch between clinical deficit and infarct, EVT offered better functional outcomes.[83] Similar favorable outcomes were demonstrated in the

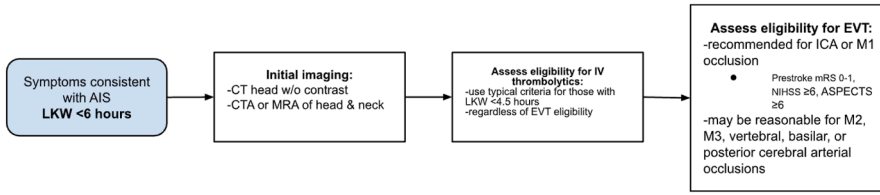
Symptoms consistent with AIS
LKW <6 hours
Initial imaging:
-CT head w/o contrast
-CTA or MRA of head & neck
Assess eligibility for IV thrombolytics:
-use typical criteria for those with LKW <4.5 hours
-regardless of EVT eligibility
Assess eligibility for EVT:
-recommended for ICA or M1 occlusion
• Prestroke mRS 0-1, NIHSS ≥6, ASPECTS ≥6
-may be reasonable for M2, M3, vertebral, basilar, or posterior cerebral arterial occlusions

Fig. 4. Proposed workflow based on last known well time less than 6 hours for determining eligibility for endovascular therapy.[39] (*From* Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2019;50(12):e344–e418. https://doi.org/10.1161/STR.0000000000000211.)

DEFUSE 3 trial where EVT was offered 6 to 16 hours from symptom onset based on perfusion imaging.[84] When caring for a patient with an LKN time between 6 and 24 hours and a confirmed LVO, perfusion imaging should be considered. Those with a favorable mismatch who meet the criteria used in either of these trials may be considered for EVT (**Fig. 5**).[39]

Large-core infarcts

Recent trials have challenged the notion that large-core strokes are not amenable to thrombectomy due to either suspected minimal benefit or risk of harm. Using non-contrast CT or CT perfusion studies to detect large-core infarcts in patients presenting within 24 hours of LKN, one study found that EVT plus standard therapy offered better functional outcomes and higher incidence of functional independence compared to standard care alone.[85] This study reported similar rates of mortality and sICH between the two groups; meanwhile, another study involving EVT in patients with large-core strokes also found a functional benefit, but with an increased risk of any ICH and sICH.[86] While awaiting more data, these studies allude to a potential upcoming shift in the management of patients with large areas of infarcted tissue that were once considered unsalvageable.

Antiplatelet Agents

Administration of 160 to 300 mg aspirin in AIS is associated with a mortality benefit and reduced rate of stroke recurrence.[87,88] While aspirin may be given in the ED, it

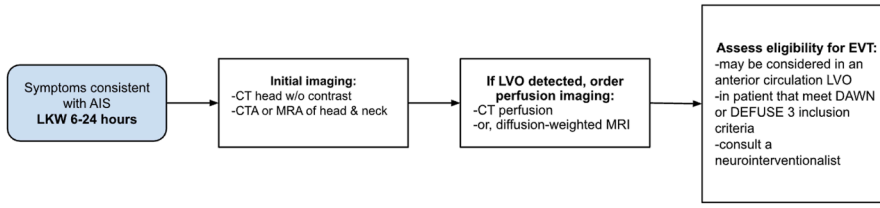
Symptoms consistent with AIS
LKW 6-24 hours
Initial imaging:
-CT head w/o contrast
-CTA or MRA of head & neck
If LVO detected, order perfusion imaging:
-CT perfusion
-or, diffusion-weighted MRI
Assess eligibility for EVT:
-may be considered in an anterior circulation LVO
-in patient that meet DAWN or DEFUSE 3 inclusion criteria
-consult a neurointerventionalist

Fig. 5. Proposed workflow based on last known well time 6 to 24 hours for determining eligibility for endovascular therapy.[39] (*From* Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2019;50(12):e344–e418. https://doi.org/10.1161/STR.0000000000000211.)

is recommended to be given within 24 to 48 hours after symptom onset and needs to be held for the initial 24 hours following IV thrombolysis.[39] Meanwhile, consultants may recommend for a patient with a transient ischemic attack (TIA) or mild ischemic stroke to be loaded with dual-antiplatelet therapy (DAPT) in the ED. One study involving patients with acute non-disabling stroke and NIHSS 5 or less found that DAPT therapy, consisting of aspirin and clopidogrel, was noninferior to r-tPA in terms of functional outcome at 90 days and even led to less risk of hemorrhage.[89] Another study found that a similar DAPT regimen confers less risk of stroke recurrence at 21 and 90 days in patients with high-risk TIA or mild ischemic stroke.[90]

SUMMARY

In an effort to curb morbidity and mortality, the management of AIS is gradually shifting paradigms from relying on time constraints to instead focusing on salvageable tissue. Beyond just a standard non-contrast CT scan, MRI is now routinely used in the ED at stroke centers to detect intervenable strokes in patients with an unclear last symptom onset who awaken with stroke symptoms. Meanwhile, accessibility to perfusion imaging in the ED allows interventionalists to visualize the vulnerable brain tissue that may be amendable to reperfusion despite a patient presenting well beyond the typical timeframe. With time, these boundaries are only likely to be further pushed including offering therapies to large territory strokes that were once considered untouchable. As clinicians at the forefront, we owe it to our patients to remain up to date with the latest innovations in stroke care in the ED.

CLINICS CARE POINTS

- When evaluating a patient with a potential ischemic stroke, the presence of visual symptoms, aphasia, and/or neglect (VAN) can help rapidly screen for a LVO.
- When performed by an experienced provider, a HINTS examination can reliably detect a posterior circulation stroke in patients presenting with continuous dizziness. Other concerning features include gait unsteadiness, unilateral hearing loss, and the "deadly D's"- diplopia, dysarthria, dysphagia, dysphonia, dysmetria, and dysesthesia.
- While the NIH Stroke Scale is highly reliable among providers and is the standard for depicting stroke severity, expect much lower numerical scores for patients exhibiting posterior circulation and/or non-dominant hemispheric strokes.
- Serum glucose is the only laboratory test required prior to administration of IV thrombolytic therapy and the remainder of tests are tailored to the specific clinical scenario.
- Consider an STAT diffusion-weighted MRI in patients who awaken with stroke symptoms yet have an unclear LKN to determine candidacy for IV thrombolytic therapy.
- Though perfusion studies may be helpful to assess a favorable ischemic core to salvageable penumbra ratio in patients with an LVO being considered for EVT, recent studies have suggested benefits of EVT even in the presence of a large core.
- In patients presenting with mild, non-debilitating stroke symptoms or a TIA, DAPT has a similar efficacy and less adverse effects as IV thrombolytics.

DISCLOSURE

The authors have nothing to disclose.

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